given the name complementary peptides. Such complementary peptides have been shown to specifically interact with their targets with moderate affinity.[18] One way to achieve this inversion of hydropathy relies on an interesting characteristic of the genetic code. That is, since A and U are complementary, and when in the middle base of the codon specifies hydrophilic and hydrophobic respectively, then the non-coding strand of DNA (or mRNA) will code for a peptide which is complementary to the peptide encoded by the coding strand. Apart from being a useful method for designing complementary peptides, this suggests a mechanism for the evolution of interacting ligand pairs. However, using this DNA-based design method does not always result in the optimal pattern of hydropathic complementarity. For this reason it has also proved useful to design complementary peptides based on the hydropathic pattern of the target peptide using computer programs.[19]

The concept of complementary peptides based on hydropathic patterns was first tested with the peptide hormone corticotropin (ACTH). A complementary peptide HTCA, was synthesized corresponding to the noncoding strand of ACTH mRNA

and tested for its ability to bind to ACTH. In a solid-phase binding assay, ACTH was found to specifically bind to this complementary peptide, HTCA, with nanomolar affinity.[20] Further, equivalent binding was observed with HTCA peptides based on a sense or antisense reading of ACTH complementary RNA.[21] The observation that these peptides had different amino acid sequences but the same linear array of hydropathy suggested that this latter property was responsible for the interaction. Additional support for the idea that inverted hydropathy is the driving force for the interaction comes from the observation that complementary peptides interact when derived from computer-assisted inversion or nucleotide sequence-directed inversion.[22]

Complementary peptides derived from molecular recognition theory have been used in a wide variety of systems as antagonists.[23-26] The present invention described the design of complementary peptides that specifically bind and alter the activity of the chemotactic ligand, N-acetyl-PGP. Since the hydropathic characteristics of proline are not very well defined, two complementary peptides to the N-acetyl-PGP were designed. One

peptide, ASA, was based on the Kyte and Doolittle scale[11] and the other peptide, RTR, was based on the Akamatsu and Fujita scale[12]. The latter is based upon the partition coefficients of di- and tri-peptides, making it more appropriate for the design of a complementary peptide to such a small target. The complementary peptides were also synthesized and tested as tetramers, a common approach used to enhance binding affinity for the target.[27,28] Multimerization increases the stoichiometry of the reaction, sequestering a greater number of chemoattractant molecules, hence reducing the dose of the complementary peptide necessary to block N-acetyl-PGP.

The inhibitory properties of the RTR complementary peptides are predicated on the molecular interaction of the RTR sequence with N-acetyl-PGP. This fact is made clear by comparing the ID_{50} values for each complementary peptide against N-acetyl-PGP. The inhibitory properties of both monomeric peptides, RTR and RTRGG (ID_{50} = 2 mM), were 20-fold less than the RTR dimer which was 500-fold less than the RTR tetramer. The ASA complementary peptide (with a polylysine core and di-glycine spacer identical to the